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               E US20060093687/PN

     FILE 'CA' ENTERED AT 11:56:40 ON 25 OCT 2007
L1             5 S VANILLOID RECEPTOR AND ROFECOXIB

     FILE 'REGISTRY' ENTERED AT 12:01:56 ON 25 OCT 2007
L2             1 S 393513-97-8/RN
                 SET NOTICE 1 DISPLAY
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     FILE 'REGISTRY' ENTERED AT 12:03:41 ON 25 OCT 2007
L3             1 S 501951-42-4/RN
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     FILE 'REGISTRY' ENTERED AT 12:04:56 ON 25 OCT 2007
L4             1 S 162011-90-7/RN
                 SET NOTICE 1 DISPLAY
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     FILE 'REGISTRY' ENTERED AT 12:43:56 ON 25 OCT 2007
L5             1 S  501951-42-4/RN
L6             1 S 162011-90-7/RN

     FILE 'CA' ENTERED AT 12:45:14 ON 25 OCT 2007
L7             6 S L5
L8          1843 S L6
L9             1 S L7 AND L8

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      31.34      73.86

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -4.38      -8.76

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 14:57:44 ON 25 OCT 2007

Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

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PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
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SESSION RESUMED IN FILE 'CA' AT 14:58:31 ON 25 OCT 2007
FILE 'CA' ENTERED AT 14:58:31 ON 25 OCT 2007
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                      31.34      73.86

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                      -4.38      -8.76

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     FILE 'CA' ENTERED AT 11:56:40 ON 25 OCT 2007
L1              5 S VANILLOID RECEPTOR AND ROFECOXIB

     FILE 'REGISTRY' ENTERED AT 12:01:56 ON 25 OCT 2007
L2              1 S 393513-97-8/RN
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     FILE 'REGISTRY' ENTERED AT 12:04:56 ON 25 OCT 2007
L4              1 S 162011-90-7/RN
                  SET NOTICE 1 DISPLAY
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     FILE 'REGISTRY' ENTERED AT 12:43:56 ON 25 OCT 2007
L5              1 S  501951-42-4/RN
L6              1 S 162011-90-7/RN

     FILE 'CA' ENTERED AT 12:45:14 ON 25 OCT 2007
L7              6 S L5
L8           1843 S L6
L9              1 S L7 AND L8

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YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y



L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   501951-42-4  REGISTRY
ED   Entered STN:  07 Apr 2003
CN   Urea, N-(2-bromophenyl)-N'-[(3R)-1-[5-(trifluoromethyl)-2-pyridinyl]-3-
     pyrrolidinyl]-  (CA INDEX NAME)
OTHER NAMES:
CN   SB 705498
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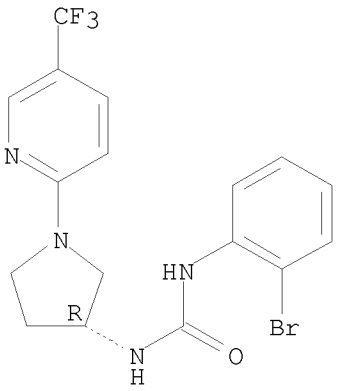
FS STEREOSEARCH
MF C17 H16 Br F3 N4 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT, EMBASE, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, SYNTHLINE, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L7 ANSWER 1 OF 6 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 147:226990 CA <<LOGINID::20071025>>
TITLE: Characterization of SB-705498, a potent and selective vanilloid receptor-1 (VR1/TRPV1) antagonist that inhibits the capsaicin-, acid-, and heat-mediated activation of the receptor
AUTHOR(S): Gunthorpe, Martin J.; Hannan, Sara Luis; Smart, Darren; Jerman, Jeffrey C.; Arpino, Sandra; Smith, Graham D.; Brough, Stephen; Wright, Jim; Egerton, Julie; Lappin, Sarah C.; Holland, Vicky A.; Winborn, Kim; Thompson, Mervyn; Rami, Harshad K.; Randall, Andrew; Davis, John B.
CORPORATE SOURCE: Neurology and Gastrointestinal Centre of Excellence for Drug Discovery, GlaxoSmithKline, Harlow, Essex, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2007), 321(3), 1183-1192
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vanilloid receptor-1 (TRPV1) is a nonselective cation channel, predominantly expressed by sensory neurons, which plays a key role in the detection of noxious painful stimuli such as capsaicin, acid, and heat. TRPV1 antagonists may represent novel therapeutic agents for the treatment of a range of conditions including chronic pain, migraine, and gastrointestinal disorders. Here we describe the in vitro pharmacol. of

N-(2-bromophenyl)-N'-[((R)-1-(5-trifluoromethyl-2-pyridyl)pyrrolidin-3-yl)]urea (SB-705498), a novel TRPV1 antagonist identified by lead optimization of N-(2-bromophenyl)-N'-{2-[ethyl(3-methylphenyl)amino]ethyl}urea (SB-452533), which has now entered clin. trials. Using a Ca2+-based fluorometric imaging plate reader (FLIPR) assay, SB-705498 was shown to be a potent competitive antagonist of the capsaicin-mediated activation of the human TRPV1 receptor (pKi = 7.6) with activity at rat (pKi = 7.5) and guinea pig (pKi = 7.3) orthologs. Whole-cell patch-clamp electrophysiol. was used to confirm and extend these findings, demonstrating that SB-705498 can potently inhibit the multiple modes of receptor activation that may be relevant to the pathophysiol. role of TRPV1 in vivo: SB-705498 caused rapid and reversible inhibition of the capsaicin (IC50 = 3 nM)-, acid (pH 5.3)-, or heat (50°; IC50 = 6 nM)-mediated activation of human TRPV1 (at -70 mV). Interestingly, SB-705498 also showed a degree of voltage dependence, suggesting an effective enhancement of antagonist action at neg. potentials such as those that might be encountered in neurons in vivo. The selectivity of SB-705498 was defined by broad receptor profiling and other cellular assays in which it showed little or no activity vs. a wide range of ion channels, receptors, and enzymes. SB-705498 therefore represents a potent and selective multimodal TRPV1 antagonist, a pharmacol. profile that has contributed to its definition as a suitable drug candidate for clin. development.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 459429-39-1D, SB-452533, derivative 501951-42-4, SB 705498
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of SB-705498, a potent and selective vanilloid receptor-1 (VR1/TRPV1) antagonist that inhibits the capsaicin-, acid-, and heat-mediated activation of receptor)

L7 ANSWER 2 OF 6 CA COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 145:76019 CA <<LOGINID::20071025>>

TITLE: Discovery of SB-705498: A potent, selective and orally bioavailable TRPV1 antagonist suitable for clinical development

AUTHOR(S): Rami, Harshad K.; Thompson, Mervyn; Stemp, Geoffrey; Fell, Steve; Jerman, Jeffrey C.; Stevens, Alexander J.; Smart, Darren; Sargent, Becky; Sanderson, Dominic; Randall, Andrew D.; Gunthorpe, Martin J.; Davis, John B.

CORPORATE SOURCE: Neurology and GI CEDD, GlaxoSmithKline, Essex, CM19 5AW, UK

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(12), 3287-3291
CODEN: BMCLE8; ISSN: 0960-894X

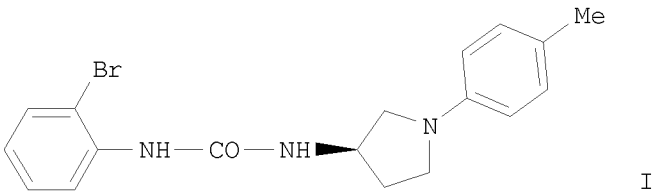
PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 145:76019

GI



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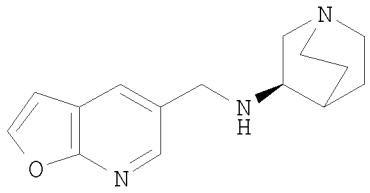

II

AB Small mol. antagonists of the vanilloid receptor TRPV1 (also known as VR1) are disclosed. Pyrrolidinyl ureas such as (I) and (II) (SB-705498) emerged as lead compds. following optimization of the previously described urea SB-452533. Pharmacol. studies using electrophysiol. and FLIPR-Ca2+-based assays showed that compds. such as I and II were potent antagonists vs. the multiple chemical and phys. modes of TRPV1 activation (namely capsaicin, acid and noxious heat). Furthermore, II possessed suitable lead compound properties to enable progression of this compound into in vivo studies and subsequently clin. development.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 501951-42-4P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SB-705498, a potent, selective and orally bioavailable TRPV1 antagonist suitable for clin. development)

L7 ANSWER 3 OF 6 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:242009 CA <<LOGINID::20071025>>
TITLE: Novel therapy for renal disorders with vanilloid receptor antagonists
INVENTOR(S): Kikkawa, Hideo; Kinoshita, Mine; Mizukami, Akiko; Ozawa, Kazunori
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005079192	A2	20050901	WO 2004-US30272	20040915
WO 2005079192	A3	20051124		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-506209P P 20030926

AB This invention relates to a novel treatment and in particular to a method for the treatment and/or prophylaxis of renal dysfunction (or disorders) associated with diseases, such as, diabetic nephropathy, glomerular nephritis, nephrosis, congestive heart failure, as well as renal dysfunctions (.apprx.r disorders) induced by drugs, including, but not limited, to antineoplastic agents, antibiotics, and immunosuppressants.

IT 501951-42-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapy for renal disorders with vanilloid receptor antagonists)

L7 ANSWER 4 OF 6 CA COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 141:99723 CA <<LOGINID::20071025>>

TITLE: Combinations of a vanilloid antagonist and an NSAID for the treatment of pain

INVENTOR(S): Bountra, Charanjit; Davis, John Beresford; Rami, Harshad Kantilal; Thompson, Mervyn

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056394	A1	20040708	WO 2003-EP14776	20031217
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AU 2003294941	A1	20040714	AU 2003-294941	20031217
EP 1572237	A1	20050914	EP 2003-785923	20031217
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JP 2006512345	T	20060413	JP 2004-561422	20031217
US 2006093687	A1	20060504	US 2005-540100	20050620
PRIORITY APPLN. INFO.:			GB 2002-29808 A	20021220
			WO 2003-EP14776 W	20031217

AB A method of treating conditions associated with pain and alleviating the symptoms associated therewith comprises administering to a mammal, including man, a vanilloid VR-1 antagonist or a pharmaceutically acceptable derivative thereof and an NSAID or a pharmaceutically acceptable derivative thereof, wherein said VR-1 antagonist or said NSAID may optionally be administered as a sub-maximal amount For example, a VR-1 antagonist, N-(2-bromophenyl)-N'-[(R)-1-(5-trifluoromethyl-2-pyridyl)pyrrolidin-3-yl)]urea (I) (preparation given), at oral dose 1 mg/kg and rofecoxib at oral dose of 1.5 mg/kg reversed a FCA-induced mech. hypersensitivity in guinea

pigs by 32.5% and 30.6%, resp. However, combination of I and rofecoxib reversed the mech. hypersensitivity by 51.8%.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 393513-97-8P 501951-42-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combinations of vanilloid antagonist and NSAID for treatment of pain)

L7 ANSWER 5 OF 6 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:264523 CA <<LOGINID::20071025>>
TITLE: Use of vanilloid receptor antagonists for the treatment of pain
INVENTOR(S): Davis, John Beresford; Winchester, Wendy Joyce
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024154	A1	20040325	WO 2003-EP10261	20030910
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003264297	A1	20040430	AU 2003-264297	20030910
EP 1545522	A1	20050629	EP 2003-795018	20030910
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JP 2006502173	T	20060119	JP 2004-535516	20030910
US 2005239846	A1	20051027	US 2005-527481	20050311
PRIORITY APPLN. INFO.:			GB 2002-21157 A	20020912
			WO 2003-EP10261 W	20030910

AB The invention discloses a method for the treatment and/or prophylaxis of pelvic pain, renal colic, biliary colic, functional dyspepsia, Barrett's metaplasia, dysphagia, and pain associated therewith, in humans or non-human mammals, which comprises the administration of an effective, non-toxic and pharmaceutically acceptable amount of a vanilloid receptor antagonist.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 501951-42-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vanilloid receptor antagonists for treatment of pain)

L7 ANSWER 6 OF 6 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 138:238029 CA <<LOGINID::20071025>>
TITLE: Preparation of ureas as vanilloid receptor (VR1) antagonists
INVENTOR(S): Rami, Harshad Kantilal; Thompson, Mervyn; Wyman, Paul

	Adrian
PATENT ASSIGNEE(S):	Smithkline Beecham P.L.C., UK
SOURCE:	PCT Int. Appl., 57 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022809	A2	20030320	WO 2002-GB4206	20020913
WO 2003022809	A3	20030717		
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CA 2458632	A1	20030320	CA 2002-2458632	20020913
AU 2002329397	A1	20030324	AU 2002-329397	20020913
EP 1425277	A2	20040609	EP 2002-765023	20020913
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BR 2002012468	A	20041019	BR 2002-12468	20020913
CN 1553905	A	20041208	CN 2002-817717	20020913
HU 2004001923	A2	20050128	HU 2004-1923	20020913
JP 2005504074	T	20050210	JP 2003-526885	20020913
NZ 531137	A	20060831	NZ 2002-531137	20020913
ZA 2004001186	A	20041029	ZA 2004-1186	20040213
IN 2004DN00473	A	20050401	IN 2004-DN473	20040227
NO 2004001003	A	20040604	NO 2004-1003	20040310
MX 2004PA02379	A	20040531	MX 2004-PA2379	20040312

PRIORITY APPLN. INFO.:	GB 2001-22156	A	20010913
	GB 2001-30503	A	20011220
	GB 2001-30505	A	20011220
	GB 2001-30547	A	20011220
	WO 2002-GB4206	W	20020913

OTHER SOURCE(S):	MARPAT 138:238029

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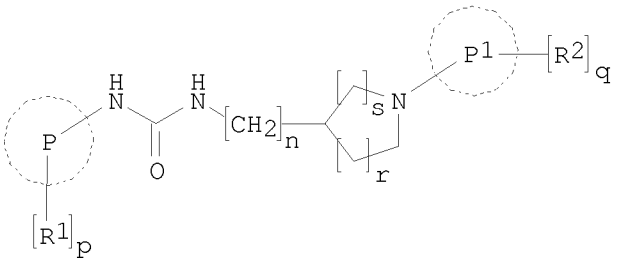

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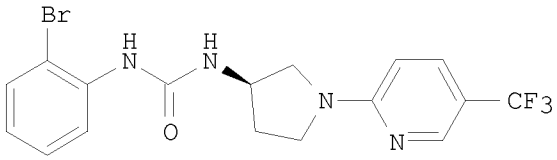

II

AB The title compds. [I; P, P1 = (hetero)aryl; R1, R2 = H, halo, alkyl, etc.; n = 0-3; p, q = 0-4; r = 1-3; s = 0-2], useful in medicine for the treatment and/or prophylaxis of pain, were prepared Thus, reacting 2-bromophenyl isocyanate with (R)-1-(5-trifluoromethylpyridin-2-yl)-pyrrolidin-3-ylamine [claimed to be prepared starting from 2-chloro-5-trifluoromethylpyridine and (3R)-3-(tert-butoxycarbonylamino)pyrrolidine; no data given] afforded (3R)-II. All compds., tested for vanilloid receptor (VR1) antagonist activity, had pKb > 6, preferred compds. having a pKb > 7.0.

IT 501951-42-4P 501951-43-5P 501951-44-6P 501951-45-7P
501951-46-8P 501951-47-9P 501951-48-0P 501951-49-1P 501951-50-4P
501951-51-5P 501951-52-6P 501951-53-7P 501951-54-8P 501951-55-9P
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501951-71-9P 501951-72-0P 501951-73-1P 501951-74-2P 501951-75-3P
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501952-06-3P 501952-07-4P 501952-08-5P 501952-09-6P 501952-10-9P
501952-11-0P 501952-12-1P 501952-13-2P 501952-14-3P 501952-15-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ureas as vanilloid receptor (VR1) antagonists for treating